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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/883,848	06/18/2001	Leona E. Ling	CIBT-P01-119	9957

28120 7590 07/10/2007

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EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
07/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/883,848	LING ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,26 and 37-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 26, 37-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/25/2007 has been entered.

Claims 1-2, 26, 37-58 are currently pending and under consideration.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 26, 37-38 and 42-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baron et al. (WO 98/35020, 1998, *of record*) in view of Porter et al. (US 6,613,798, 2003, *of record*).

Baron et al. teach a method of treating a subject suffering from an ischemia in tissues containing mesodermally derived cells comprising administering a compound to the ischemic site so as to stimulate vascular growth, wherein the ischemia is myocardial ischemia and the compound is an agonist of a hedgehog-protein-receptor (page 5, lines 1-5 and page 53, lines 20-30). With regards to the compounds, the WO document teach that compounds of the invention include, but are not limited to, molecules which interact with membrane proteins which initiate signal transduction pathways such as smoothened, patched and gli which regulate hematopoiesis and vascular growth; and include, but are not limited to, hedgehog proteins and synthetic agonists (page 17, line 26 to page 18, line 7).

Baron et al. do not explicitly teach that the synthetic agonist is a hedgehog agonist having the formula XII with a molecular weight of less than 750 amu. Nor does Baron et al. teach that the compound is administered systemically.

Porter et al teach small organic agonist that are capable of promoting proliferation in cells by modulating the hedgehog pathway, wherein the small organic agonists encompasses the claimed small organic compounds of formula XII, as well as the claimed substituents claimed in Claims 43-57 and molecular weight (column 6, formula I, column 19, lines 3-10 and Column 7, lines 5 to lines 65). With regards to the hedgehog pathway, the patent teaches that the small organic agonist can modulate the signal transduction pathway regulated by hedgehog, pathched (ptc), gli and/or smoothened (column 18, lines 40-43). Moreover, Porter et al. teach (column 54, lines 19-25) that the small organic agonist may be administered to a patient suffering from severe congestive heart failure (CHF) characterized by cardiac cachexia, as well as for promoting wound healing resulting from surgery, wherein the wound heals with less scarring (column 61, lines 8-27). With regards to the administration, the patent teaches that the agonist may be administered systemically at a dosage of 0.0001 to about 100 mg per kilogram (column 67, lines 1-8 and lines 46-59).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the references so as to use the specifically taught small organic agonists taught by Porter et al. in the method of treating a subject suffering from myocardial ischemia as taught by Baron et al.. One would have been motivated to do so because Porter et al. teach that the small organic agonist modulate the signal transduction pathway regulated by hedgehog, pathched (ptc), gli and/or smoothened (column 18, lines 40-43). Thus, one or ordinary skill in the art would have a reasonable expectation of success that by administering small organic hedgehog agonist as taught by Porter et al., one would achieve an treating a subject suffering from an myocardial ischemia.

Claims 39-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baron et al. (WO 98/35020, 1998, *of record*) in view of Porter et al. (US 6,613,798, 2003, *of record*), as applied above to claims 1-2, 26, 37-38 and 42-58, and in further view of Igo et al. (US 5,681,278, 1997, *of record*).

Baron et al. in view of Porter et al. teach a method of treating a subject suffering from an ischemia in tissues containing mesodermally derived cells comprising systemically administering a compound to the ischemic site so as to stimulate vascular growth, wherein the ischemia is myocardial ischemia and the compound is an hedgehog agonist encompassed by the instantly claimed compounds of Formula XIII.

Baron et al. in view of Porter et al. do not explicitly teach that the agonist is administered by direct injection to ischemic myocardium, intrapericardial administration or by intracoronary catheter delivery.

Igo et al. teach method for treating blood vessels in a mammal, especially the coronary blood vessels (abstract). Specifically, the patent teaches that the blood vessels can be treated by administering an agent intracoronarally to reopen the thrombosed vessel and reduce the incidence of myocardial infarction or intrapericardial injection (column 3, lines 9-16 and column 6, lines 21-22). With regards to intrapericardial injection, Igo et al. teach that many agents have been injected into the pericardial space allowing for a site specific delivery of the agent which attains higher, longer lasting drug levels in the pericardial fluid with lower plasma concentrations and less systemic toxicity (column 6, lines 23-28).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to optimize the routes of administration of the hedgehog agonist as taught by Baron et al in view of Porter et al. for the treatment of a patient following myocardial infarction. One would have been motivated to do so because it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A. Moreover, as taught by Igo et al., intrapericardial administration allows for a site specific delivery of the agent which attains higher, longer lasting drug levels in the pericardial fluid with lower plasma concentrations and less systemic toxicity. Thus, one or ordinary skill in the art would have a reasonable expectation of success that by optimizing the administration routes of the hedgehog agonist as taught by Baron et al. in view of Porter et al., one would achieve an method of selectively targeting the blood vessels of a patient following myocardial infarction.

In response to these rejections, Applicants assert that the instant claims are drawn to a method of increasing VEGF expression. As such, Applicants assert that none of Baron et al., Porter et al., or Pettet et al. teach or suggest that an agonist of the hedgehog pathway can induce expression of VEGF. Furthermore, Applicants assert that any rejection based on the alleged inherent expression of VEGF or an alleged inherent relationship between VEGF and hedgehog is insufficient to support a rejection under 35 USC 103 because VEGF expression does not necessarily and invariably occur during angiogenesis.

These arguments have been carefully considered, but are not found persuasive.

Regarding Applicants assertions that neither Baron et al., Porter et al., or Pettet et al. teach or suggest that an agonist of the hedgehog pathway can induce expression of VEGF, the Examiner acknowledges and concedes that none of the references teach inducing VEFG expression. However, the Examiner recognizes that the fact that Applicants have recognized another advantage, e.g., induce expression of VEGF, which would flow naturally from following the suggestion of the prior art, e.g., administration of a hedgehog agonist for the treatment of myocardial ischemia, cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985

Therefore, No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brandon J Fetterolf, PhD
Patent Examiner
Art Unit 1642

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